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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/227,742

Applicant(s)

BLOOM ET AL.

Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 45-47, 49-59, 61-82 and 85-91 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 45-47, 49-59, 61-71, 81 and 82 is/are allowed.
- 6) ☒ Claim(s) 72-77, 80, 85-88 and 91 is/are rejected.
- 7) ☒ Claim(s) 78, 79, 89 and 90 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Receipt is acknowledged of a response filed 9/26/2003. No changes to the specification or claims were specified in applicants' response. The arguments presented therein concerning the rejection of claims under 35 U.S.C. 112 1st paragraph were fully considered, but not found persuasive for reasons indicated below.

This action is FINAL.

Oath/Declaration

Applicants' arguments concerning the need to submit a supplemental Oath/Declaration made in the response filed 9/26/03 were persuasive. The objection of record to the Oath/Declaration is withdrawn.

Drawings

The drawings were received on 9/26/2003. These drawings are accepted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72-77, 80, 85-88, 91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new grounds of rejection that was not necessitated by applicants' amendment of the claims in Paper No. 32.**

The rejected claims are directed towards transformation competent *E. coli* cells possessing a membrane having an increased unsaturated fatty acid content relative to total fatty acid content where the *E. coli* cells exhibit enhanced transformation ability relative to the transformation ability exhibited by the competent *E. coli* cells prior to increasing their unsaturated fatty acid content (e.g. claim 72). The increased fatty acid content can be caused by the enhanced expression of one or more genes that encode one or more gene products that increase the unsaturated fatty acid content (e.g. claims 73 and 85). The increased fatty acid can be selected from oleic acid, linoleic acid, palmitoleic acid and cis-vaccenic acid (e.g. claim 76). The competent cell can be obtained following genetic selection or by recombinant means. The genes involved in increased unsaturated fatty acid content for the cell membrane can be literally **any** of the genes in the cell that contributes in **any** way to an increase in unsaturated fatty acid content in the membrane, even **indirectly**. The rejected claims thus embrace an extremely large genus of gene products that can act directly or indirectly to increase the unsaturated fatty acid content of the *E. coli* cell membrane, and consequently increase the cell viability and/or transformation of the cell. The broadest claims (e.g. claims 72 and 85) further embrace any cells that have simply been cultured under conditions that metabolically induce changes in the fatty acid content of the cell, without necessarily any genetic manipulation or selection. In addition, the cells embraced by the rejected claims include those where the increased unsaturated fatty

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acid content is due to the expression of genes heterologous to *E. coli* whose gene products somehow result in an increase in the level of unsaturated fatty acid content of the cell membrane.

The instant specification teaches a single embodiment wherein an *E. coli* strain was selected for its ability to withstand storage for prolonged periods of time at a relatively high temperature (i.e. SB3499). This strain was not further characterized as to the mutation or mutations involved in generating the increased unsaturated fatty acid content of the cell membrane. The specification further teaches working examples that demonstrate that an alteration in the expression levels of a single gene, *fabB*, can result in an increase in the levels of unsaturated fatty acid in the *E. coli* cell membrane. The specification further recites a series of specific genes known in the art to be involved in unsaturated fatty acid biosynthesis (i.e. *fabB*, *fabF*, *fabD*, *fabG*, *fabA*, *fabI*, *fabZ*, *fadA*, *fadB*, *fadE*, *fadL*, *fadR*, *farR* and a *fatA* gene (page 14, lines 1-4).

Methods of making competent cells having an improved viability and/or transformation efficiency of bacteria by increasing the unsaturated fatty acid content of their cellular membrane appears to be novel in the art. While *E. coli* is one of the most metabolically and genetically characterized of bacteria, the rejected claims are so broad in scope as to encompass cells comprising any modification in the expression of any gene that directly or **indirectly** increases the content of unsaturated fatty acids in the membrane of the cells. Given the extreme breadth of the claims, even the recitation of some of the known genes involved in the biosynthesis of unsaturated fatty acids in *E. coli* and some knowledge of the fatty acid composition of its membrane in general, one of skill in the art wouldn't have the means to identify a sufficient number of specific embodiments to describe the broadly claimed genus of cells obtained by

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selection, recombinant engineering or even differing culture conditions. Therefore, one of skill in the art would have reasonably concluded applicants were not in possession of the claimed invention.

Response to Arguments

Applicant's arguments filed in the response of 9/26/2003 have been fully considered but they are not persuasive. The response essentially argues: 1) the skilled artisan would appreciate that the invention includes E. coli having an increased unsaturated fatty acid content and that the increase could be accomplished by genetic or non-genetic methods, 2) the specification indicates that the genetic modifications can affect fatty acid content directly or indirectly, 3) the concept of indirect mutations was well-established in the field of bacterial genetics, 4) the specification provides working examples of E. coli that have been manipulated to have increase fatty acid content (e.g. an extra copy of the fabB gene), and 5) the specification teaches an additional working example (e.g. E. coli strain SB3499) which possesses a membrane having an increased unsaturated fatty acid content and that exhibits enhanced transformation ability where the strain was obtained by selection.

The examiner agrees that the rejected claims read on an enormous genus of different E. coli strains (e.g. literally any gene or gene product modification in the cells which increases the unsaturated fatty acid content of the cells). Embodiments embraced by the rejected claims include, for example, those wherein the composition of the cells is changed solely due to culture conditions. In this case, the actual fatty acid content is likely to be different from that of, for example, SB3349 or one of the fabB embodiments. Thus, a recitation that the claimed competent cells have an increased unsaturated fatty acid content relative to fatty acid content

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prior to some manipulation is merely a recitation of a desired outcome, without providing a structural/function basis for the skilled artisan to envision the claimed embodiments. With regard to the arguments directed to the description provided by the instant application (e.g. SB3499, etc.), as indicated above, the claimed genus is so broad in scope that the few examples provided by the instant specification cannot be considered as providing a basis to envision the broadly claimed genus. For example, SB3349 has not been further characterized as to the genetic modifications resulting in its increased unsaturated fatty acid content. It cannot provide descriptive support except as to what the content of a single embodiment of the invention might look like as far as membrane content. This single example of what the membrane of a cell embraced by the rejected claims might look like cannot be considered as providing a basis to envision a representative number of other embodiments. For example, looking at applicants' own data, there are significant compositional differences between the different strains used in their experiments (e.g. Table 4, DH5 α and DH10B). The fact that one can select for strains having an increased unsaturated fatty acid content does not provide a basis for the skilled artisan to envision a sufficient number of specific embodiments in order to describe the broadly claimed genus of *E. coli* strains.

Conclusion

Claims 45-47, 49-59, 61-82, 85-91 are pending. Claims 72-77, 80, 85-88, 91 are rejected. Claims 78-79, 89-90 are objected to as being dependent on a rejected claim, but would be allowable if rewritten in independent form comprising each of the limitations upon which they are currently dependent. Claims 45-47, 49-59, 61-71, 81-82 are allowed.

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr., PhD
Primary Examiner
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GERRY LEFFERS
PRIMARY EXAMINER

Ggl